Cost-effectiveness and clinical efficacy of biliary stents in patients undergoing neoadjuvant therapy for pancreatic adenocarcinoma in a randomized controlled trial

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Background and Aims: The optimal type of stent for the palliation of malignant biliary obstruction in patients with pancreatic adenocarcinoma undergoing neoadjuvant chemoradiotherapy with curative intent is unknown. We performed a prospective trial comparing 3 types of biliary stents—fully covered self-expandable metal (fcSEMS), uncovered self-expandable metal (uSEMS), and plastic—to determine which best optimized cost-effectiveness and important clinical outcomes.

Methods: In this prospective randomized trial, consecutive patients with malignant biliary obstruction from newly diagnosed pancreatic adenocarcinoma who were to start neoadjuvant chemoradiotherapy were randomized to receive fcSEMSs, uSEMSs, or plastic stents during the index ERCP. The primary outcomes were time to stent occlusion, attempted surgical resection, or death after the initiation of neoadjuvant therapy, and the secondary outcomes were total patient costs associated with the stent, including the index ERCP cost, downstream hospitalization cost due to stent occlusion, and the cost associated with procedural adverse event.

Results: Fifty-four patients were randomized and reached the primary end point: 16 in the fcSEMS group, 17 in the uSEMS group, and 21 in the plastic stent group. No baseline demographic or tumor characteristic differences were noted among the groups. The fcSEMSs had a longer time to stent occlusion compared with uSEMSs and plastic stents (220 vs 74 and 76 days, $P < .01$), although the groups had equivalent rates of stent occlusion, attempted surgical resection, and death. Although SEMS placement cost more during the index ERCP (uSEMS = \$24,874 and fcSEMS = \$22,729 vs plastic = \$18,701; $P < .01$), they resulted in higher procedural AE costs per patient (uSEMS = \$5522 and fcSEMS = \$12,701 vs plastic = \$0; $P < .01$). Conversely, plastic stents resulted in an \$11,458 hospitalization cost per patient due to stent occlusion compared with \$2301 for uSEMSs and \$0 for fcSEMSs ($P < .01$).

Conclusions: In a prospective trial comparing fcSEMSs, uSEMSs, and plastic stents for malignant biliary obstruction in patients undergoing neoadjuvant therapy with curative intent for pancreatic adenocarcinoma, no stent type was superior in optimizing cost-effectiveness, although fcSEMSs resulted in fewer days of neoadjuvant treatment delay and a longer time to stent occlusion. (Clincial trial registration number: NCT01038713.) (Gastrointest Endosc 2016;84:460-6.)

Abbreviations: AE, adverse event; fcSEMS, fully covered self-expandable metal stent; IV, intravenously; PEP, post-ERCP pancreatitis; SEMS, self-expandable metal stent; uSEMS, uncovered self-expandable metal stent.

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Extrahepatic malignant biliary obstruction due to pancreatic adenocarcinoma requires palliation if the patient is not deemed to be a candidate for upfront surgical resection.[1,2] In addition, patients who undergo neoadjuvant therapy with planned surgical curative intent must be palliated for the 5 to 6 months before resection.[3] For these patients, treatment consists of placing a temporary plastic or self-expandable metal stent (SEMS) to relieve clinical symptoms and allow for normalization of liver test results so that neoadjuvant therapy can be given.[4]

Although SEMSs seem to be the optimal stent type for patients deemed to be unresectable given their better patency rates, the optimal stent type in patients undergoing neoadjuvant therapy is controversial.[5,6] Along with their better patency rates, SEMSs have a higher periprocedural adverse event (AE) rate and cost more than plastic stents.[7] Thus, although SEMSs have better patency rates than plastic stents, their effectiveness may be offset by associated increases in downstream health-related and economic costs. In the specific population of patients with malignant biliary obstruction undergoing neoadjuvant therapy with curative intent, plastic stents may actually be more advantageous due to less overall cost and fewer AEs such as treatment delay.

We performed a prospective, comparative effectiveness trial evaluating 3 types of biliary stents—fully-covered self-expandable metal (fcSEMS), uncovered self-expandable metal (uSEMS), and plastic—to determine which best optimized cost-effectiveness and important clinical outcomes in patients undergoing neoadjuvant therapy. A priori, we predicted that plastic stents would be as cost-effective as SEMSs regarding total patient costs associated with the stent, including index ERCP costs, downstream hospitalization costs due to stent occlusion, and costs associated with procedural AEs.

METHODS

Study design

We enrolled patients at a single tertiary care academic medical center in the United States from February 2010 to April 2013 after receiving approval from the Committee for the Protection of Human Subjects, Dartmouth College (Hanover, NH) on December 9, 2009. Additional study monitoring was performed by the Norris Cotton Cancer Center (Dartmouth-Hitchcock Medical Center, Lebanon, NH) Data Safety Monitoring and Accrual Committee. The study was registered at ClincialTrials.gov (number NCT01038713) and reported under the auspices of the CONSORT guidelines.[8]

Patients

All patients were adults able to provide written informed consent. Patients were included if they were referred for ERCP (with or without EUS) at Dartmouth-Hitchcock Medical Center for palliation of extrahepatic malignant biliary obstruction due to pancreatic adenocarcinoma. At the time of enrollment, all patients had cross-sectional imaging suggestive of resectable, borderline, or locally unresectable invasive pancreatic ductal adenocarcinoma before their ERCP as defined by the Americas Hepato-Pancreato-Biliary Association convened consensus conference on pancreatic cancer.[9] Patients were required to have clinical, radiographic, and cross-sectional imaging findings consistent with extrahepatic biliary obstruction requiring stent placement. If, at the time of ERCP and/or EUS, patients were deemed to have disease that would not potentially benefit from neoadjuvant therapy by being downstaged to resectable disease, they were excluded from the study. All participants must have had planned follow-up at our institution; patients with planned neoadjuvant therapy at another institution were excluded. Patients in whom stent placement could not be performed were not included in the study. All patients had verified pancreatic adenocarcinoma via FNA or exploratory laparoscopy.

Randomization

Randomization was conducted during the ERCP after biliary access had been obtained with an access wire based on a web-based random number generator. All patients who had wire access achieved were subsequently able to have a stent placed. Neither the endoscopist nor the patient was blinded to the randomization assignment.

Intervention

Procedures were performed by 1 of 2 experienced therapeutic endoscopists with the patient under conscious or monitored anesthesia. After successful bile duct cannulation and wire placement, patients were randomized to receive an fcSEMS, uSEMS, or plastic stent. Both SEMSs were 10-mm WallFlex stents of varying lengths (6, 8, and 10 cm) (Boston Scientific, Marlborough, Mass), and plastic stents were 10F Cotton-Leung stents (7, 9, and 12 cm) (Cook Endoscopy, Winston-Salem, NC). The length of the stent was chosen at the discretion of the treating endoscopist. All procedure-related maneuvers and interventions were managed by the attending endoscopist. Multiple stents were not placed in any of the patients. Routine overnight observation of patients after ERCP was not performed.

Neoadjuvant therapy

After stent placement, patients were referred to the Dartmouth Multidisciplinary Pancreas tTumor Clinic, where a neoadjuvant treatment protocol was initiated. All patients underwent neoadjuvant chemoradiotherapy using 1 of 3 chemoradiotherapy regimens. Patients eligible for an ongoing clinical trial received cetuximab 400 mg/m^2 intravenously (IV) once followed by 250 mg/m^2 IV weekly and gemcitabine 50 mg/m^2 IV biweekly over 6 weeks